Abstract

Method and materials are provided for screening for genetic polymorphism in a test population of DNA fragments. Heteroduplexes are formed between members a test DNA population and their corresponding complements from a reference DNA population. Perfectly matched heteroduplexes are destroyed or separated from those containing mismatched sequences. Preferably, perfectly matched heteroduplexes are digested by a single stranded exonuclease which requires double stranded DNA as a substrate, such as E. coli exonuclease III. Amplicons are formed from mismatched heteroduplexes, preferably by extending the partially digested duplexes after treatment with exonuclease III followed by PCR amplification. The resulting amplicons are inserted into a cloning vector which is used to transform a bacterial host. After host cells are plated and allowed to form colonies, clones are picked and sequenced to identify DNA fragments containing polymorphic sequences.